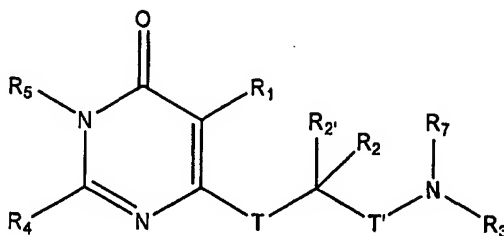


What is claimed is:

1. A compound selected from the group represented by Formula I:



Formula I

wherein:

T and T' are independently a covalent bond or optionally substituted lower alkylene;

R₁ is chosen from hydrogen, optionally substituted alkyl, optionally substituted aryl, optionally substituted aralkyl, optionally substituted heteroaryl, and optionally substituted heteroaralkyl;

R₂ and R_{2'} are independently chosen from hydrogen, optionally substituted alkyl, optionally substituted aryl, optionally substituted aralkyl, optionally substituted heteroaryl, and optionally substituted heteroaralkyl; or R₂ and R_{2'} taken together form an optionally substituted 3- to 7-membered ring;

R₃ is chosen from hydrogen, optionally substituted alkyl-, optionally substituted aryl-, optionally substituted aralkyl-, optionally substituted heteroaryl-, optionally substituted heteroaralkyl-, -C(O)-R₆, and -S(O)₂-R_{6a};

R₄ is independently chosen from hydrogen, optionally substituted alkyl, optionally substituted alkoxy, hydroxyl, nitro, cyano, dialkylamino, alkylsulfonyl, alkylsulfonamido, alkylthio, carboxyalkyl, carboxamido, aminocarbonyl, optionally substituted aryl, optionally substituted aralkyl, optionally substituted heteroaralkyl and optionally substituted heteroaryl; and

R₅ is hydrogen, optionally substituted alkyl, optionally substituted aryl, optionally substituted aralkyl, optionally substituted heteroaryl, or optionally substituted heteroaralkyl; or

R₄ taken together with R₅ form an optionally substituted 5 to 7-membered ring nitrogen-containing heterocycle, which optionally incorporates from one to two additional heteroatoms, selected from N, O, and S in the heterocycle ring;

R₆ is chosen from hydrogen, optionally substituted alkyl, optionally substituted aryl, optionally substituted aralkyl, optionally substituted heteroaryl, optionally substituted heteroaralkyl, R₁₁O- and R₁₂-NH-;

R_{6a} is chosen from optionally substituted alkyl, optionally substituted aryl, optionally substituted alkylaryl, optionally substituted heteroaryl, optionally substituted alkylheteroaryl, and R₁₂-NH-;

R₇ is chosen from hydrogen, optionally substituted alkyl, optionally substituted aryl, optionally substituted aralkyl, optionally substituted heteroaryl, and optionally substituted heteroaralkyl;

or R₇ taken together with R₃, and the nitrogen to which they are bound, form an optionally substituted 5- to 12-membered nitrogen-containing heterocycle, which optionally incorporates from one to two additional heteroatoms, selected from N, O, and S in the heterocycle ring;

or R₇ taken together with R₂ form an optionally substituted 5- to 12-membered nitrogen-containing heterocycle, which optionally incorporates from one to two additional heteroatoms, selected from N, O, and S in the heterocycle ring;

R₁₁ is chosen from optionally substituted alkyl, optionally substituted aryl, optionally substituted aralkyl, optionally substituted heteroaryl, and optionally substituted heteroaralkyl; and

R₁₂ is chosen from hydrogen, optionally substituted alkyl, optionally substituted aryl, optionally substituted aralkyl, optionally substituted heteroaryl, and optionally substituted heteroaralkyl;

a pharmaceutically acceptable salt of a compound of Formula I;
a pharmaceutically acceptable solvate of a compound of Formula I; or
a pharmaceutically acceptable solvate of a pharmaceutically acceptable salt of a compound of Formula I.

2. A compound of claim 1 comprising one or more of the following:
one of T and T' is absent and the other is optionally substituted alkylene;
R₁ is selected from optionally substituted lower alkyl, optionally substituted aryl, or

optionally substituted aralkyl;

R₂ is optionally substituted C₁-C₄ alkyl;

R_{2'} is hydrogen or optionally substituted C₁-C₄ alkyl;

R₃ is -C(O)R₆;

R₆ is selected from optionally substituted C₁-C₈ alkyl, optionally substituted aryl-C₁-C₄-alkyl-, optionally substituted heteroaryl-C₁-C₄-alkyl-, optionally substituted heteroaryl, optionally substituted aryl, R₁₁O- and R₁₂-NH-;

R₁₁ is chosen from optionally substituted C₁-C₈ alkyl and optionally substituted aryl;

R₁₂ is chosen from hydrogen, optionally substituted C₁-C₈ alkyl and optionally substituted aryl;

R₇ is chosen from hydrogen, C₁-C₄ alkyl; cyclohexyl; phenyl substituted with hydroxyl, C₁-C₄ alkoxy or C₁-C₄ alkyl; benzyl; and R₁₆-alkylene-;

R₁₆ is hydroxyl, carboxy, (C₁-C₄ alkoxy)carbonyl-, di(C₁-C₄ alkyl)amino-, (C₁-C₄ alkyl)amino-, amino, (C₁-C₄ alkoxy)carbonylamino-, C₁-C₄ alkoxy-, or optionally substituted N-heterocycl- (particularly azetidyl, morpholyl, pyridyl, indolyl, furanyl, pyrrolidyl, piperidyl or imidazolyl, each of which may be optionally substituted;

R₄ is chosen from hydrogen, hydroxyl, lower alkyl (particularly methyl), lower alkoxy (particularly methoxy) and cyano; and

R₅ is chosen from hydrogen, lower alkyl (particularly methyl), and aralkyl (particularly benzyl).

3. A compound of claim 2 comprising one or more of the following:

T and T' are absent;

R₁ is chosen from ethyl, propyl, methoxyethyl, naphthyl, phenyl, bromophenyl, chlorophenyl, methoxyphenyl, ethoxyphenyl, tolyl, dimethylphenyl, chlorofluorophenyl, methylchlorophenyl, ethylphenyl, phenethyl, benzyl, chlorobenzyl, methylbenzyl, methoxybenzyl, cyanobenzyl, hydroxybenzyl, dichlorobenzyl, dimethoxybenzyl, naphthylmethyl, and (ethoxycarbonyl)ethyl;

R₂ is hydrogen;

R₂ is optionally substituted C₁-C₄ alkyl;

R₆ is chosen from phenyl; phenyl substituted with one or more of the following substituents: halo; C₁-C₄ alkyl; C₁-C₄ alkyl substituted with hydroxy (e.g., hydroxymethyl); C₁-C₄ alkoxy; C₁-C₄ alkyl substituted with C₁-C₄ alkoxy, halo, nitro, formyl, carboxy,

cyano, methylenedioxy, ethylenedioxy, acyl (e.g., acetyl), -N-acyl (e.g., N-acetyl) or trifluoromethyl; benzyl; phenoxymethyl-; halophenoxymethyl-; phenylvinyl-; heteroaryl-; heteroaryl- substituted with C₁-C₄ alkyl or C₁-C₄ alkyl substituted with halo (e.g., CF₃); C₁-C₄ alkyl substituted with C₁-C₄ alkoxy-; and benzyloxymethyl-;

R₇ is chosen from hydrogen, methyl, ethyl, propyl, butyl, cyclohexyl, carboxyethyl, carboxymethyl, methoxyethyl, hydroxyethyl, hydroxypropyl, dimethylaminoethyl, dimethylaminopropyl, diethylaminoethyl, diethylaminopropyl, aminopropyl, methylaminopropyl, 2,2-dimethyl-3-(dimethylamino)propyl, aminoethyl, aminobutyl, aminopentyl, aminohexyl, isopropylaminopropyl, diisopropylaminoethyl, 1-methyl-4-(diethylamino)butyl, (t-Boc)aminopropyl, hydroxyphenyl, benzyl, methoxyphenyl, methylmethoxyphenyl, dimethylphenyl, tolyl, ethylphenyl, (oxopyrrolidinyl)propyl, (methoxycarbonyl)ethyl, benzylpiperidinyl, pyridinylethyl, pyridinylmethyl, morpholinylethyl, morpholinylpropyl, piperidinyl, azetidinylmethyl, azetidinylethyl, azetidinypropyl, pyrrolidinylethyl, pyrrolidinylpropyl, piperidinylmethyl, piperidinylethyl, imidazolylpropyl, imidazolethyl, (ethylpyrrolidinyl)methyl, (methylpyrrolidinyl)ethyl, (methylpiperidinyl)propyl, (methylpiperazinyl)propyl, furanylmethyl and indolyethyl; and

R₄ is hydrogen, optionally substituted alkyl, optionally substituted aryl, alkoxy, cyano, substituted amino, carbamyl, aryloxy, heteroaryloxy, heteroaryl, optionally substituted N-heterocyclyl, or trifluoromethyl.

4. A compound of claim 3 comprising one or more of the following:

R₁ is chosen from ethyl, propyl, methoxyethyl, naphthyl, phenethyl, benzyl, chlorobenzyl, methylbenzyl, methoxybenzyl, cyanobenzyl, hydroxybenzyl, dichlorobenzyl, dimethoxybenzyl, naphthylmethyl, and (ethoxycarbonyl)ethyl;

R₂ is chosen from methyl, ethyl, propyl, butyl, methylthioethyl, methylthiomethyl, aminobutyl, (CBZ)aminobutyl, cyclohexylmethyl, benzyloxymethyl, methylsulfinylethyl, methylsulfinylmethyl, and hydroxymethyl;

R₆ is chosen from phenyl, halophenyl, dihalophenyl, cyanophenyl, halo(trifluoromethyl)phenyl, hydroxymethyl-phenyl, methoxymethylphenyl, methoxyphenyl, ethoxyphenyl, carboxyphenyl, formylphenyl, ethylphenyl, tolyl, methylenedioxyphenyl, ethylenedioxyphenyl, methoxychlorophenyl, methylhalophenyl, trifluoromethylphenyl, furanyl, C₁-C₄ alkyl substituted furanyl, trifluoromethylfuranyl, C₁-C₄ alkyl substituted trifluoromethylfuranyl, benzofuranyl, thiophenyl, C₁-C₄ alkyl substituted thiophenyl,

benzothiophenyl, benzothiadiazolyl, pyridinyl, indolyl, methylpyridinyl, trifluoromethylpyridinyl, pyrrolyl, quinolinyl, picolinyl, pyrazolyl, C₁-C₄ alkyl substituted pyrazolyl, N-methyl pyrazolyl, C₁-C₄ alkyl substituted N-methyl pyrazolyl, C₁-C₄ alkyl substituted pyrazinyl, C₁-C₄ alkyl substituted isoxazolyl, benzoisoxazolyl, morpholinomethyl, methylthiomethyl, methoxymethyl, N-methyl imidazolyl, and imidazolyl;

R₇ is R₁₆-alkylene-; and

R₁₆ is amino, C₁-C₄ alkylamino-, di(C₁-C₄ alkyl)amino-, C₁-C₄ alkoxy-, hydroxyl, or N-heterocyclyl.

5. A compound of claim 4 comprising one or more of the following:

R₁ is benzyl, chlorobenzyl, methylbenzyl, methoxybenzyl, cyanobenzyl, or hydroxybenzyl;

R₂ is ethyl or propyl;

R₆ is optionally substituted phenyl (especially, tolyl, halophenyl, methylhalophenyl, hydroxymethyl-phenyl, halo(trifluoromethyl)phenyl-, methylenedioxyphenyl, formylphenyl or cyanophenyl); and

R₁₆ is amino.

6. A compound of claim 1 comprising one or more of the following:

one of T and T' is absent and the other is optionally substituted alkylene;

R₁ is selected from optionally substituted lower alkyl, optionally substituted aryl, or optionally substituted aralkyl;

R₂ is optionally substituted C₁-C₄ alkyl;

R₂' is hydrogen or optionally substituted C₁-C₄ alkyl;

R₃ is -C(O)R₆;

R₆ is selected from optionally substituted C₁-C₈ alkyl, optionally substituted aryl-C₁-C₄-alkyl-, optionally substituted heteroaryl-C₁-C₄-alkyl-, optionally substituted heteroaryl, optionally substituted aryl, R₁₁O- and R₁₂-NH-;

R₁₁ is chosen from optionally substituted C₁-C₈ alkyl and optionally substituted aryl;

R₁₂ is chosen from hydrogen, optionally substituted C₁-C₈ alkyl and optionally substituted aryl;

R₇ is chosen from hydrogen, C₁-C₄ alkyl; cyclohexyl; phenyl substituted with hydroxyl, C₁-C₄ alkoxy or C₁-C₄ alkyl; benzyl; and R₁₆-alkylene-;

R₁₆ is hydroxyl, carboxy, (C₁-C₄ alkoxy)carbonyl-, di(C₁-C₄ alkyl)amino-, (C₁-C₄ alkyl)amino-, amino, (C₁-C₄ alkoxy)carbonylamino-, C₁-C₄ alkoxy-, or optionally substituted N-heterocyclyl- (particularly azetidiny, morpholinyl, pyridinyl, indolyl, furanyl, pyrrolidinyl, piperidinyl or imidazolyl, each of which may be optionally substituted; and

R₄ and R₅ taken together form an optionally substituted 5 to 7-membered nitrogen-containing heterocycle which optionally incorporates from one to two additional heteroatoms, selected from N, O, and S in the heterocycle ring.

7. A compound of claim 6 comprising one or more of the following:

T and T' are absent;

R₁ is chosen from ethyl, propyl, methoxyethyl, naphthyl, phenyl, bromophenyl, chlorophenyl, methoxyphenyl, ethoxyphenyl, tolyl, dimethylphenyl, chlorofluorophenyl, methylchlorophenyl, ethylphenyl, phenethyl, benzyl, chlorobenzyl, methylbenzyl, methoxybenzyl, cyanobenzyl, hydroxybenzyl, dichlorobenzyl, dimethoxybenzyl, naphthylmethyl, and (ethoxycarbonyl)ethyl;

R₂ is hydrogen;

R₂ is optionally substituted C₁-C₄ alkyl;

R₆ is chosen from phenyl; phenyl substituted with one or more of the following substituents: halo; C₁-C₄ alkyl; C₁-C₄ alkyl substituted with hydroxy (e.g., hydroxymethyl); C₁-C₄ alkoxy; C₁-C₄ alkyl substituted with C₁-C₄ alkoxy, halo, nitro, formyl, carboxy, cyano, methylenedioxy, ethylenedioxy, acyl (e.g., acetyl), -N-acyl (e.g., N-acetyl) or trifluoromethyl; benzyl; phenoxymethyl-; halophenoxymethyl-; phenylvinyl-; heteroaryl-; heteroaryl- substituted with C₁-C₄ alkyl or C₁-C₄ alkyl substituted with halo (e.g., CF₃); C₁-C₄ alkyl substituted with C₁-C₄ alkoxy-; and benzyloxymethyl-;

R₇ is chosen from hydrogen, methyl, ethyl, propyl, butyl, cyclohexyl, carboxyethyl, carboxymethyl, methoxyethyl, hydroxyethyl, hydroxypropyl, dimethylaminoethyl, dimethylaminopropyl, diethylaminoethyl, diethylaminopropyl, aminopropyl, methylaminopropyl, 2,2-dimethyl-3-(dimethylamino)propyl, aminoethyl, aminobutyl, aminopentyl, aminohexyl, isopropylaminopropyl, diisopropylaminoethyl, 1-methyl-4-(diethylamino)butyl, (t-Boc)aminopropyl, hydroxyphenyl, benzyl, methoxyphenyl, methylmethoxyphenyl, dimethylphenyl, tolyl, ethylphenyl, (oxopyrrolidinyl)propyl, (methoxycarbonyl)ethyl, benzylpiperidinyl, pyridinylethyl, pyridinylmethyl, morpholinylethyl, morpholinylpropyl, piperidinyl, azetidinylmethyl, azetidinyethyl, azetidinypropyl

pyrrolidinylethyl, pyrrolidinylpropyl, piperidinylmethyl, piperidinylethyl, imidazolylpropyl, imidazolethyl, (ethylpyrrolidinyl)methyl, (methylpyrrolidinyl)ethyl, (methylpiperidinyl)propyl, (methylpiperazinyl)propyl, furanylmethyl and indolyethyl; and

R₄ and R₅ taken together form an optionally substituted pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, piperidinyl, piperazinyl, hexahydropyrimidinyl, piperazinyl, morpholinyl, pyrrolyl, pyrazolyl, imidazolyl, dihydroisoxazolyl, or dihydrooxazolyl ring.

8. A compound of claim 1 comprising one or more of the following:

one of T and T' is absent and the other is optionally substituted alkylene;

R₁ is selected from optionally substituted lower alkyl, optionally substituted aryl, or optionally substituted aralkyl;

R₂ is optionally substituted C₁-C₄ alkyl;

R₂' is hydrogen or optionally substituted C₁-C₄ alkyl;

R₃ taken together with R₇ and the nitrogen to which they are bound, forms an optionally substituted imidazolyl; and

R₄ is chosen from hydrogen, hydroxyl, lower alkyl, lower alkoxy and cyano; and R₅ is chosen from hydrogen, lower alkyl, and aralkyl; or R₄ and R₅ taken together form an optionally substituted 5 to 7-membered nitrogen-containing heterocycle which optionally incorporates from one to two additional heteroatoms, selected from N, O, and S in the heterocycle ring.

9. A compound of claim 1 comprising one or more of the following:

one of T and T' is absent and the other is optionally substituted alkylene;

R₁ is selected from optionally substituted lower alkyl, optionally substituted aryl, or optionally substituted aralkyl;

R₂ is optionally substituted C₁-C₄ alkyl;

R₂' is hydrogen or optionally substituted C₁-C₄ alkyl;

R₃ taken together with R₇ and the nitrogen to which they are bound, forms an optionally substituted imidazolyl; and

R₄ is chosen from hydrogen, hydroxyl, lower alkyl, lower alkoxy and cyano; and R₅ is chosen from hydrogen, lower alkyl, and aralkyl; or R₄ and R₅ taken together form an optionally substituted 5 to 7-membered nitrogen-containing heterocycle which optionally incorporates from one to two additional heteroatoms, selected from N, O, and S in the heterocycle ring.

10. A compound of claim 1 comprising one or more of the following:
one of T and T' is absent and the other is optionally substituted alkylene;
R₁ is selected from optionally substituted lower alkyl, optionally substituted aryl, or optionally substituted aralkyl;
R₂ is optionally substituted C₁-C₄ alkyl;
R_{2'} is hydrogen or optionally substituted C₁-C₄ alkyl;
R₃ taken together with R₇ and the nitrogen to which they are bound, forms an optionally substituted diazepinone; and
R₄ is chosen from hydrogen, hydroxyl, lower alkyl, lower alkoxy and cyano; and R₅ is chosen from hydrogen, lower alkyl, and aralkyl; or R₄ and R₅ taken together form an optionally substituted 5 to 7-membered nitrogen-containing heterocycle which optionally incorporates from one to two additional heteroatoms, selected from N, O, and S in the heterocycle ring.
11. A compound of claim 1 wherein:
R₁ is benzyl, chlorobenzyl, methylbenzyl, methoxybenzyl, cyanobenzyl, or hydroxybenzyl;
R_{2'} is hydrogen;
R₂ is optionally substituted C₁-C₄ alkyl;
R₃ is -C(O)R₆;
R₆ is optionally substituted phenyl;
R₇ is R₁₆-alkylene-;
R₁₆ is amino, C₁-C₄ alkylamino-, di(C₁-C₄ alkyl)amino-, C₁-C₄ alkoxy-, hydroxyl, or N-heterocyclyl;
R₄ is chosen from hydrogen, hydroxyl, lower alkyl (particularly methyl), lower alkoxy (particularly methoxy) and cyano; and
R₅ is chosen from hydrogen, lower alkyl (particularly methyl), and aralkyl (particularly benzyl).
12. A compound of claim 1 wherein:
R₁ is benzyl, chlorobenzyl, methylbenzyl, methoxybenzyl, cyanobenzyl, or hydroxybenzyl;
R_{2'} is hydrogen;
R₂ is optionally substituted C₁-C₄ alkyl;

R_3 is $-C(O)R_6$;

R_6 is $R_{12}NH-$;

R_{12} is chosen from hydrogen, C_1 - C_4 alkyl; cyclohexyl; and optionally substituted phenyl;

R_7 is R_{16} -alkylene-,

R_{16} is amino, C_1 - C_4 alkylamino-, di(C_1 - C_4 alkyl)amino-, C_1 - C_4 alkoxy-, hydroxyl, or N-heterocyclyl;

R_4 is chosen from hydrogen, hydroxyl, lower alkyl (particularly methyl), lower alkoxy (particularly methoxy) and cyano; and

R_5 is chosen from hydrogen, lower alkyl (particularly methyl), and aralkyl (particularly benzyl).

13. A compound of claim 1 wherein:

R_1 is benzyl, chlorobenzyl, methylbenzyl, methoxybenzyl, cyanobenzyl, or hydroxybenzyl;

R_2 is hydrogen;

R_2 is optionally substituted C_1 - C_4 alkyl;

R_3 is $-C(O)R_6$;

R_6 is $R_{11}O-$;

R_{11} is chosen from optionally substituted C_1 - C_8 alkyl and optionally substituted aryl;

R_7 is R_{16} -alkylene-;

R_{16} is amino, C_1 - C_4 alkylamino-, di(C_1 - C_4 alkyl)amino-, C_1 - C_4 alkoxy-, hydroxyl, or N-heterocyclyl;

R_4 is chosen from hydrogen, hydroxyl, lower alkyl (particularly methyl), lower alkoxy (particularly methoxy) and cyano; and

R_5 is chosen from hydrogen, lower alkyl (particularly methyl), and aralkyl (particularly benzyl).

14. A compound of claim 1 that is

N-(3-Amino-propyl)-N-[1-(5-benzyl-2-methyl-6-oxo-1,6-dihydro-pyrimidin-4-yl)-2-methyl-propyl]-4-methyl-benzamide;

N-(3-Amino-propyl)-N-[1-(5-benzyl-1,2-dimethyl-6-oxo-1,6-dihydro-pyrimidin-4-yl)-2-methyl-propyl]-4-methyl-benzamide;

N-(3-Amino-propyl)-N-[1-(3-benzyl-4-oxo-4H-pyrido[1,2-a]pyrimidin-2-yl)-2-methyl-propyl]-4-methyl-benzamide; or

N-(3-Amino-propyl)-N-[1-(3-benzyl-8-chloro-4-oxo-4H-pyrido[1,2-a]pyrimidin-2-yl)-2-methyl-propyl]-4-methyl-benzamide.

15. A compound of any of the above claims wherein the stereogenic center to which R₂ and R₂' is attached is of the R configuration.

16. A composition comprising a pharmaceutical excipient and a compound, salt, or solvate thereof of any one of claims 1-14.

17. A composition according to claim 16, wherein said composition further comprises a chemotherapeutic agent other than a compound of Formula I or a pharmaceutical salt or solvate thereof.

18. A composition according to claim 17 wherein said composition further comprises a taxane.

19. A composition according to claim 17, wherein said composition further comprises a vinca alkaloid.

20. A composition according to claim 17, wherein said composition further comprises a topoisomerase I inhibitor.

21. A method of modulating KSP kinesin activity which comprises contacting said kinesin with an effective amount of a compound according to any one of claims 1 to 13, or a pharmaceutically acceptable salt or solvate thereof.

22. A method of inhibiting KSP which comprises contacting said kinesin with an effective amount of a compound according to any one of claims 1 to 13, or a pharmaceutically acceptable salt or solvate thereof.

23. A method for the treatment of a cellular proliferative disease comprising

administering to a subject in need thereof a compound according to any one of claims 1-13, or a pharmaceutically acceptable salt or solvate thereof.

24. A method for the treatment of a cellular proliferative disease comprising administering to a subject in need thereof a composition according to any one of claims 16-20.

25. A method according to claim 23 or claim 24 wherein said disease is selected from the group consisting of cancer, hyperplasias, restenosis, cardiac hypertrophy, immune disorders, and inflammation.

26. The use, in the manufacture of a medicament for treating cellular proliferative disease, of a compound according to any one of claims 1-13, or a pharmaceutically acceptable salt or solvate thereof

27. The use of a compound as defined in claim 26 for the manufacture of a medicament for treating a disorder associated with KSP kinesin activity.